General

Guideline Title

Candidiasis. In: British HIV Association and British Infection Association guidelines for the treatment of opportunistic infection in HIV-seropositive individuals 2011.

Bibliographic Source(s)

Cartledge J, Freedman A. Candidiasis. In: British HIV Association and British Infection Association guidelines for the treatment of opportunistic infection in HIV-seropositive individuals 2011. HIV Med. 2011 Sep;12(Suppl 2):70-4. [46 references]

Guideline Status

This is the current release of the guideline.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- January 4, 2016 – Noxafil (posaconazole) : The U.S. Food and Drug Administration (FDA) is cautioning that differences in dosing regimens between the two oral formulations of the antifungal Noxafil (posaconazole) have resulted in dosing errors. To help prevent additional medication errors, the drug labels were revised to indicate that the two oral formulations cannot be directly substituted for each other but require a change in dose. Direct mg for mg substitution of the two formulations can result in drug levels that are lower or higher than needed to effectively treat certain fungal infections.

Recommendations

Major Recommendations

Level of evidence (I–IV) ratings are defined at the end of the "Major Recommendations" field.

Diagnosis

- Oral and oesophageal candidiasis are clinical diagnoses (IV).

- Microbiological confirmation and susceptibility testing of *Candida* species (spp) is required when symptoms of candidiasis persist or develop whilst the patient is taking antifungal therapy (IV).
- Oesophageal candidiasis can be diagnosed clinically if oropharyngeal candidiasis is present (IV).
- Confirmation by endoscopy can be reserved for cases with symptoms of oesophageal candidiasis who fail to respond to initial therapy, do not have concomitant oropharyngeal candidiasis or those in which an additional oesophageal condition is suspected (IIb).

Treatment

- Azoles and topical treatment are equally effective at treating oropharyngeal candidiasis but azole therapy is associated with a lower risk of relapse (Ib).
- Voriconazole, posaconazole or the echinocandins (caspofungin, micafungin and anidulafungin) should be reserved for cases in which the organism is resistant to fluconazole but sensitive to the newer agent, to cases which fail to respond clinically to fluconazole despite sensitivity or where the individual is intolerant of fluconazole therapy (IV).
- There are no clinical trial data to guide the treatment of invasive candidiasis in human immunodeficiency virus (HIV)-seropositive individuals. In general, they should be treated with systemic antifungal therapy as in other immunocompromised patients (IV).

Prophylaxis

- Routine prophylaxis is not warranted and is associated with the emergence of resistance (III).

Definitions:

Level of Evidence

Ia	Evidence obtained from meta-analysis of randomized controlled trials
Ib	Evidence obtained from at least one randomized controlled trial
IIa	Evidence obtained from at least one well designed controlled study without randomization
IIb	Evidence obtained from at least one other type of well designed quasi-experimental study
III	Evidence obtained from well designed non-experimental descriptive studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Oropharyngeal, oesophageal, and vaginal candidiasis
  - *Candida albicans* infection
  - Non-albicans *Candida* infection
- Human immunodeficiency virus (HIV) seropositivity

Guideline Category

Diagnosis

Management

Treatment

Clinical Specialty

Family Practice

Gastroenterology

Infectious Diseases

Internal Medicine

Obstetrics and Gynecology

Otolaryngology

Pathology

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To help physicians in the United Kingdom investigate and manage human immunodeficiency virus (HIV)-seropositive patients suspected of or having candidiasis

Target Population

Human immunodeficiency virus (HIV)-seropositive patients suspected of or having candidiasis

Interventions and Practices Considered

Diagnosis

1. Clinical diagnosis (signs and symptoms)
2. Microbiological confirmation
3. Susceptibility testing
4. Endoscopy for cases with symptoms of oesophageal candidiasis

Treatment

1. Azoles: fluconazole, ketoconazole, itraconazole, voriconazole, posaconazole, clotrimazole
2. Topical treatment
3. Echinocandins: caspofungin, micafungin and anidulafungin

Note: Routine prophylaxis was considered but not recommended.

Major Outcomes Considered

- Rate of yeast clearance
- Efficacy rate
- Relapse rate
- Response rate

- Resolution of infection
- Adverse events related to therapy
- Development of drug resistance

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The PubMed database was searched under the following headings: HIV or AIDS and candidosis, candidiasis, *Candida* spp, *Candida albicans*, non-albicans Candida, oropharyngeal candidiasis and mucosal candidiasis.

All information considered had to have been published in a peer review journal or presented at an international human immunodeficiency virus (HIV) meeting in abstract form. Inclusion/exclusion criteria essentially required that the information was relevant to the diagnosis, treatment or prevention of the specified opportunistic infection in HIV-positive individuals. Information of relevance to other related immunocompromised groups was also taken into consideration if the section authors felt relevant. Case reports were included and the review was not restricted only to clinical trials or meta-analyses. Search dates were from 1980 to January 2011.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Level of Evidence

Ia	Evidence obtained from meta-analysis of randomized controlled trials
Ib	Evidence obtained from at least one randomized controlled trial
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Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Accurate diagnosis and appropriate treatment of candidiasis in human immunodeficiency virus (HIV)-seropositive individuals

Potential Harms

- Azoles can cause hepatitis; it is advisable to use fluconazole, as the least hepatotoxic agent, in patients with liver disease.
- There are rare reports of candidiasis associated with immune reconstitution inflammatory syndrome (IRIS), including a case of *Candida* meningitis leading to fatal vasculitis.
- Refer to Table 7.1 in the original guideline document for interactions between drugs used to treat *Candida* infection and antiretroviral drugs.
- Refer to Appendix 1 in the original guideline document for side effects of certain drug formulations.

Contraindications

Contraindications

- Ketoconazole is teratogenic in laboratory animals, is contraindicated in pregnancy and like other azoles can cause hepatitis.
- Refer to Appendix 1 in the original guideline document for contraindications of certain drug formulations.

Qualifying Statements

Qualifying Statements

- These guidelines are primarily intended to guide practice in the United Kingdom and related health systems. Although it is hoped they can provide some guidance in developed countries there are some important distinctions in this environment and individual recommendations may not be as applicable in this setting.
- In the appendices in the original guideline document there is an A–Z of drugs used in the management of opportunistic infections. This is intended as a guideline but readers are advised to follow the discussion of dosing and the evidence for specific treatments provided in the text. In some cases alternative treatments are provided in the appendix in the original guideline document. These are not discussed in the text and these are mainly of historical interest and readers should be aware that these are not, in general, supported by the evidence base for treatments discussed in the text. It should also be noted that as evidence of drug toxicity, interactions, pregnancy risk and cost is rapidly evolving the table should be considered in association with the updated summary of product characteristics (SPC) for the agent and other relevant sources of drug information.
- Recommendations based upon expert opinion have the least evidence but perhaps provide an important reason for writing the guidelines: to produce a consensual opinion about current practice. It must, however, be appreciated that such opinion is not always correct and alternative practices may be equally valid. The recommendations contained in these guidelines should therefore be viewed as guidelines in the true spirit of the term. They are not designed to be restrictive nor should they challenge research into current practice. Similarly, although the British HIV Association (BHIVA) Opportunistic Infection Guidelines Group seeks to provide guidelines to optimize treatment, such care needs to be individualized and the authors have not constructed a document that they would wish to see used as a 'standard' for litigation.
- The clinical care of patients with known or suspected opportunistic infections (OIs) requires a multidisciplinary approach, drawing on the skills and experience of all healthcare professional groups. Moreover, these guidelines emphasize that inpatients with human immunodeficiency virus (HIV)-related disease often need rapid access to a variety of diagnostic tests and radiological interventions that may not be immediately available at local hospitals. Furthermore, expert interpretation of these tests by supporting specialties such as radiology, histopathology, microbiology and virology is often required. Optimal care of opportunistic infection can only be achieved by the close cooperation of these healthcare professionals and unless all are intimately involved in the care of patients, it is likely that the outcome will be less favourable. In keeping with BHIVA standards for HIV clinical care, patients needing inpatient care for HIV-related disease should ordinarily be admitted to an HIV centre or the relevant tertiary service in liaison with the HIV centre.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Sep

Guideline Developer(s)

British HIV Association - Disease Specific Society

British Infection Association - Professional Association

Source(s) of Funding

British HIV Association

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Financial Disclosures/Conflicts of Interest

The British HIV Association (BHIVA) has a clear policy of declarations of interests within the Association:

- BHIVA requires that all members of guidelines writing groups, as well as any expert external peer reviewers, must declare all interests and membership of other committees retrospectively on an annual basis, to give protection to individuals working as members of writing groups.
- All members of guidelines writing groups must undertake a declaration of interests prior to serving on a writing group and this declaration is confirmed and repeated at the publication of each set of completed guidelines published.
- The details given in declaration forms are retained on a register at the Secretariat and can be made available for publication, if required.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the British HIV Association (BHIVA) Web site . Also available as a smartphone app from the BHIVA Web site .

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 30, 2014. This summary was updated by ECRI Institute on January 6, 2016 following the U.S. Food and Drug Administration advisory on Noxafil (posaconazole).

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